CRPPA gene

CDP-L-ribitol pyrophosphorylase A

Normal Function

The *CRPPA* gene provides instructions for making a protein that is involved in a process called glycosylation. Through this chemical process, sugar molecules are added to certain proteins. In particular, the CRPPA protein helps produce a molecule called ribitol 5-phosphate, which is an important component of the chain of sugar molecules added to a protein called alpha (α)-dystroglycan. Glycosylation is critical for the normal function of α-dystroglycan.

The α-dystroglycan protein helps anchor the structural framework inside each cell (cytoskeleton) to the lattice of proteins and other molecules outside the cell (extracellular matrix). In skeletal muscles, glycosylated α-dystroglycan helps stabilize and protect muscle fibers. In the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

Health Conditions Related to Genetic Changes

Walker-Warburg syndrome

At least 17 mutations in the *CRPPA* gene have been found to cause Walker-Warburg syndrome, the most severe form of a group of disorders known as congenital muscular dystrophies. Walker-Warburg syndrome causes skeletal muscle weakness and abnormalities of the brain and eyes. Because of the severity of the problems caused by this condition, affected individuals usually do not survive past early childhood.

CRPPA gene mutations involved in Walker-Warburg syndrome prevent the normal glycosylation of α-dystroglycan. As a result, α-dystroglycan can no longer effectively anchor cells to the proteins and other molecules that surround them. Without functional α-dystroglycan to stabilize the muscle fibers, they become damaged as they repeatedly contract and relax with use. The damaged fibers weaken and die over time, which affects the development, structure, and function of skeletal muscles in people with Walker-Warburg syndrome.

Defective α-dystroglycan also affects the migration of neurons during the early development of the brain. Instead of stopping when they reach their intended destinations, some neurons migrate past the surface of the brain into the fluid-filled space that surrounds it. Researchers believe that this problem with neuronal migration causes a brain abnormality called cobblestone lissencephaly, in which the

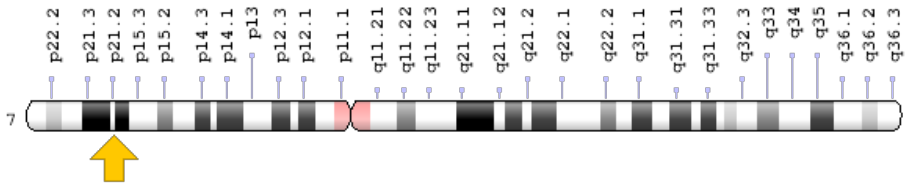
surface of the brain lacks the normal folds and grooves and instead appears bumpy and irregular. Less is known about the effects of *CRPPA* gene mutations on other parts of the body.

Limb-girdle muscular dystrophy

Chromosomal Location

Cytogenetic Location: 7p21.2, which is the short (p) arm of chromosome 7 at position 21.2

Molecular Location: base pairs 16,087,525 to 16,421,538 on chromosome 7 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase-like protein
- 4-diphosphocytidyl-2C-methyl-D-erythritol synthase homolog
- hCG_1745121
- isoprenoid synthase domain containing
- isoprenoid synthase domain-containing protein
- IspD
- ISPD
- ISPD_HUMAN
- MDDGA7
- Nip
- notch1-induced protein

Additional Information & Resources

Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Protein Glycosylation in the ER and Golgi Complex
  https://www.ncbi.nlm.nih.gov/books/NBK21744/
- Washington University Neuromuscular Disease Center
  https://neuromuscular.wustl.edu/syncm.html#ispd

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ISPD%5BTIAB%5D%29+OR+%28IspD%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ISOPRENOID SYNTHASE DOMAIN-CONTAINING PROTEIN
  http://omim.org/entry/614631

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ISPD.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CRPPA%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:37276
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:729920
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/729920
- UniProt
  https://www.uniprot.org/uniprot/A4D126

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